REMARKS

By this paper, claims 15, 19 and 43 have been amended. Claims 14-28 and 39-44 remain pending.

112 Rejection

In the December 19, 2005 Office action, claims 1-28 and 39-44 were rejected under 35 U.S.C. § 112, first paragraph. In so rejecting the claims, the Examiner stated that the specification of the present application, "while being enabling for the use of certain inhibitors of TGFβ for the inhibition of cataract or after cataract formation, does not reasonably provide enablement for the use of all inhibitors of TGFβ for the inhibition of such disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims." (See Page 2 of January 26, 2005 Office action). Additionally, in the outstanding Office action, the Examiner stated that claims 14-28 and 39-44 were rejected under § 112, first paragraph, as failing to comply with the written description requirement because the pending claims contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention."

In response to the rejections of the claims under § 112, first paragraph, the Applicants have submitted with this response a declaration by Professor Antony Wilks Burgess, a person of ordinary skill in the field of growth factors and their actions on cells. Professor Burgess has been working in the field of growth factors and their actions on cells since 1976, well before the priority date claimed for the present application.

The enclosed declaration clearly demonstrates that:

1. on or before November 19, 1993, the expression "inhibitors of TGFβ" had a clear meaning to one of ordinary skill in the art;

2. on or before November 19, 1993, one of ordinary skill in the art could have readily established whether a particular compound was an inhibitor of TGFβ using assays well known in the art;

3. in the November 19, 1993 time frame, one of ordinary skill in the art, having the benefit of reviewing the specification of the present application, could have readily confirmed that a particular inhibitor of TGFβ inhibits the cataract-like changes to lens cells induced by TGFβ, and therefore the inhibitor could be used to inhibit TGFβ-induced cataract or after cataract formation in the eye.

Notably, the present application does not claim inhibitors of TGFβ per se, but does claim certain methods of treatment that comprise administering one or more inhibitors of TGFβ, and certain formulations comprising one or more inhibitors of TGFβ.

Claims 14 to 18 of the present application claim a method of inhibiting TGFβ-induced cataract or after cataract formation in the eye of a mammalian subject in need of such inhibition, which comprises the step of administering to the subject an effective amount of one or more inhibitors of TGFβ. Claims 24 to 28 claim a method of inhibiting after cataract formation in the eye of a mammalian subject following lens implant surgery, which comprises the step of implanting in the eye of the subject a lens coated with one or more inhibitors of TGFβ. Claims 19 to 23 and 39 to 44 claim certain formulations comprising one or more inhibitors of TGFβ.

As described in the specification of the present application, the inventors have surprisingly and unexpectedly found that TGFβ induces lens cells to undergo changes that characteristically occur during the formation of various types of cataract and after cataract (see

page 13, lines 15 to 29 of the specification), and have further found that these changes can be inhibited by inhibitors of TGFβ (see page 14, line 34 to page 15, line 7 and page 20, lines 3 to 10 of the specification).

Example 1 in the specification describes an experiment which clearly demonstrates that TGFβ induces lens cells to undergo changes that characteristically occur during the formation of various types of cataract and after cataract. This was surprising and unexpected as there was no suggestion in the art before November 19, 1993 that TGFβ may be involved in the formation of cataract or after cataract.

Examples 2 and 4 in the specification demonstrate that two very different types of inhibitors of TGFβ (an antibody against TGFβ and α_2 - macroglobulin) inhibit the TGFβ-induced changes in lens cells.

Accordingly, the specification provides experimental data demonstrating that TGFβ induces lens cells to undergo changes that characteristically occur during the formation of various types of cataract and after cataract, and demonstrating that two very different types of inhibitors of TGFβ (an antibody against TGFβ and α_2 - macroglobulin) inhibit these changes.

Prior to November 19, 1993, TGFβ, and other growth factors, were well known in the art. The structure of TGFβ and its receptors were described in the art, as evidenced by the enclosed declaration. An example of a publication describing TGFβ is "Transforming growth factor βs : chemistry, biology, and therapeutics." Annals of the New York Academy of Sciences, Volume 593, Karl A. Piez and Michael B. Sporn, editors, New York: The New York Academy of Sciences, 1990, 379 pages. Before November 19, 1993, a person of ordinary skill in the art would have understood the term "inhibitor of TGFβ" to refer to any compound that inhibits the

biological activity of TGFβ. Numerous compounds that inhibit the activity of TGFβ had been described in the art before November 19, 1993.

In the Office Action, the Examiner has cited the following authorities:

- Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997). cert. Denied, 523 U.S. 1089 S.Ct. 1548 (1998);
- Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d, 316 1324 25 (Fed. Cir. 2002);
- Univ. of Rochester v. G.D. Searle & Co., Inc., 249 F. supp. 2d 216.225 (W.D.N.Y.2003).

These authorities clearly establish that "Compliance with the written description requirement is essentially a fact based enquiry that will 'necessarily vary depending on the nature of the invention claimed'" (Enzo 296 F.3d at 1324 citing In re DiLeone).

These authorities also clearly establish that functional descriptions can meet the written description requirement. For example, Enzo 296 F.3d at 1324 stated that "it is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement". That decision indicated that the written description requirement may be met by an invention defined by functional characteristics when coupled with a known or disclosed correlation between function and structure. As an example of such a case, the decision referred to the "Synopsis of Application of Written Description Guidelines" of the USPTO at page 60 which indicated that a claim in the terms of "An isolated antibody capable of binding to antigen X" would satisfy the written description requirement. That section in the "Synopsis of Application of Written Description Guidelines" considered that such a claim satisfied the written description requirement as the functional characteristics of antibody binding and the structural characteristics for antibodies were well defined in the art and the relevant technology was well

developed and mature, and therefore one of ordinary skill in the art would recognize that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

In relation to Univ. of Rochester v. G.D. Searle & Co., Inc., we note that this case concerned a claim to a method for selectively inhibiting PGHS-2 activity in a human host where the activity of PGHS-1 is not inhibited. In that case, it was found that the claims did not satisfy the written description requirement. A significant part of the Court's reasoning was that the specification failed to identify a single compound with the relevant activity, and therefore the Court considered that the specification did not set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed.

In clear contrast, the present application refers to a known class of compounds (inhibitors of TGFβ), refers to certain specific compounds that are inhibitors of TGFβ, and provides experimental data demonstrating that the inventors were in possession of the invention claimed at the time the application was filed.

Applying the reasoning of the above authorities, we submit the specification clearly satisfies the written description requirement.

The authorities referred to above clearly indicate that the mere fact that a feature of an invention is defined by function does not mean the claim fails to satisfy the written description requirement. The functional characteristic of acting to inhibit TGFβ is coupled with the well known structure of TGFβ and its receptors. Further, it is the standard practice in the medical field to describe compounds by reference to their activity.

As evidenced by the Burgess declaration filed herewith, a person of ordinary skill in the art before November 19, 1993 would readily understand what is meant by the expression "inhibitor of TGFβ" and could readily identify compounds that have that activity.

Further, the specification of the present application provides experimental evidence that demonstrates that TGFβ inhibitors act to inhibit the TGFβ -induced changes in lens cells.

Further, as evidenced by the enclosed Burgess declaration, a person of ordinary skill in the art, using standard assays known in the art before November 19, 1993, could determine whether a particular compound was an inhibitor of TGFβ. As discussed at length in the response to the Office Action of January 26, 2005, one assay that could be used is the test using mink lung epithelial cells described in numerous prior art documents (we refer the Examiner to the detailed discussion of this assay in that response). Another assay referred to in the enclosed declaration is an assay using African green monkey kidney epithelial (BSC-1) cells.

As demonstrated by the Examples in the subject specification, the inventors have found that TGFβ induces changes in lens cells that characteristically occur in certain forms of cataract and after cataract, and have demonstrated that inhibiting TGFβ inhibits the TGFβ -induced changes. Accordingly, the inventors have demonstrated that any compound which acts to inhibit the activity of TGFβ (i.e. any inhibitor of TGFβ) may be used.

In the telephone interview with the Examiner on May 9, 2006, the Examiner queried whether a person of ordinary skill in the art could determine whether a particular inhibitor of TGFβ inhibited the TGFβ -induced changes in lens cells. As evidenced by the enclosed Burgess declaration, a person of ordinary skill in the art, having the benefit of reviewing the specification of the subject application, could readily confirm that a particular inhibitor of TGFβ inhibits the

TGFβ -induced changes in lens cells by a lens explant study such as that described in the Examples in the specification.

We submit it is clear from the information in the specification that, at the time the application was filed, the inventors were in possession of the invention claimed. The inventors have not only demonstrated that TGFβ induces changes in lens cells that characteristically occur in certain forms of cataract and after cataract, but have also provided in the specification experimental evidence, using two different inhibitors of TGFβ, that inhibitors of TGFβ inhibit these changes.

We further submit that the specification provides sufficient detail to enable a person of ordinary skill in the art to perform the invention as broadly claimed. The specification refers to various inhibitors of TGFβ that may be used, for example, at page 2 lines 4 to 12. Further, experiments using two specific inhibitors of TGFβ are discussed in Examples 2 and 4 of the specification. In addition, other inhibitors of TGFβ could readily be identified by a person of ordinary skill in the art by a literature search for compounds having that activity. Further, whether a particular compound has that activity could readily be assessed by routine standard assays.

In the Office Action, the Examiner has stated that "The instant specification, quite simply, cannot provide direction for using any peptides, proteins or RNA-DNA based structures, in the absence of any identifying characteristics of any kind, e.g. sequences". In relation to this comment, we submit that the application does not claim the use of any peptide, protein or RNA-DNA based structure. The application claims the use of one or more inhibitors of TGFβ. The claims only encompass the use of peptides, proteins or RNA-DNA based structures if the

peptide, protein or RNA-DNA based structure used in the claimed method is an inhibitor of TGFβ.

In this regard, claim 15, for example, refers to the method of claim 14 wherein the one or more inhibitors of TGFβ are "selected from proteins, glycoproteins or proteoglycans". This is a dependent claim, and includes all the features of claim 14. Claim 14 is limited to a method which comprises the step of administering one or more inhibitors of TGFβ. Claim 15 is directed to that method, wherein the inhibitor of TGFβ happens to be a protein, glycoprotein or proteoglycan. Administration of a protein, glycoprotein or proteoglycan that is not an inhibitor of TGFβ would not fall within the scope of claim 15. The specification does not suggest that all proteins, glycoproteins and proteoglycans inhibit TGFβ. We further note that the claims clearly refer to the identifying characteristic of the relevant compounds, namely, that the compounds are inhibitors of TGFβ.

The Examiner has also stated that "The instant claims read on 'inhibitors of TGFβ' necessitating an exhaustive search for the embodiment suitable to practice the claimed invention". In this regard, we note that it would not be necessary to conduct an exhaustive search for an embodiment suitable to practice the claimed invention. Any inhibitor of TGFβ may be used in the method of the invention. Suitable inhibitors of TGFβ are described in the specification (e.g. the antibody referred to in Example 2 or α_2 - macroglobulin referred to in Example 4). Further, inhibitors of TGFβ are described in the prior art. Further, as evidenced by the enclosed declaration, a person of ordinary skill in the art could readily determine whether a particular compound was an inhibitor of TGFβ by routine assays known in the art.

We also note, for the Examiner's information, that various granted US patents claim methods defined by reference to compounds which influence the biological activity of TGFβ,

further demonstrating that it is standard practice in the medical field to refer to compounds by their biological activity. For example:

- US 6,673,341 defines a method referring to the use of "an anti-TGF-β antibody".
- US 6,166,090 defines a method which comprises administering "a therapeutic agent to increase the level of TGF-beta".
- US 5,958,411 defines a method comprising administering "an agent that binds to TGF-β".
- US 5,599,844 refers to a method comprising administration of "an agent effective upon oral administration to elevate the level of TGF-beta".

Accordingly, it is respectfully submitted that claims 1-28 and 39-44 satisfy the requirements of § 112 and can be passed to issue.

102(b) Rejection

In relation to the rejection of claims 19 to 23 in view of WO 92/17206, claim 19 has been amended. WO 92/17206 does not describe any ophthalmological formulations, and certainly does not describe an ophthalmological formulation formulated for topical application to the eye as defined by amended claim 19.

As a person of ordinary skill in the art would be aware, the fluids that normally bathe the eye and lens have very specific properties that should be mimicked in solutions that are applied to the eye. For example, the medium used as the vehicle for delivering an active agent in eye drops to the surface of the eye should resemble the tear fluid that normally bathes the surface of the eye (see, for example, Bachman WG and Wilson G. Invest Ophthalmal Vis Sci. 1985; 26: 1484-1488; Gilbard PG, Rossi SR. and Gray Heyda K. Am. J Ophthalmol. 1989; 107: 348-355).

We respectfully submit that WO 92/17206 does not describe an ophthalmological formulation formulated for topical application to the eye and, therefore, we submit that claims 19 to 23 are novel over WO 92/17206.

CONCLUSION

In view of the above remarks, Applicants respectfully request that the application be reconsidered, the claims allowed and the application passed to issue.

Respectfully submitted,

FULWIDER PATTON LLP

By: _____
John V. Hanley
Registration No. 38,171

JVH/kst
Howard Hughes Center
6060 Center Drive, Tenth Floor
Los Angeles, CA 90045
Telephone: (310) 824-5555
Facsimile: (310) 824-9696
Customer No. 24201
129664.1